MIGRATION, MINES AND MORES:
THE HIV EPIDEMIC IN SOUTHERN AFRICA

INAUGURAL ADDRESS: PROF JOHN HARGROVE NOV 2007

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ABOUT THE AUTHOR

John Hargrove was born near Glasgow, Scotland, in 1946, but was taken by his family to Southern Rhodesia where he had all of his schooling in Bulawayo. Having developed an early interest in ornithology he studied zoology at Pembroke College, Oxford (1965-1968). Finding little support for research in ornithology in Rhodesia he embarked on a study of the physiology of flight in tsetse flies (*Glossina* spp), receiving a PhD from the University of London in 1973. From 1974-1978 he worked for the government's Tsetse and Trypanosomiasis Control Branch with Dr Glyn Vale, a working relationship that continues to this day. Research carried out in the Zambezi Valley centred on the development of effective, low-cost, ecologically friendly methods of tsetse control. John played an early part in identifying odour attractants, designing new traps, studying fly behaviour and movement and population dynamics.

The field research rekindled an interest in mathematics and led him to the Biomathematics Department at the University of California in Los Angeles. John then rejoined the tsetse group in the Zambezi Valley, working for the Zimbabwe Government from 1981-1986 and thereafter on British-funded tsetse projects until 1998. He continued working on population dynamics and in other theoretical areas in support of the efficient application of bait methods of tsetse control, which were now being applied on a large scale in Zimbabwe and elsewhere.

In 1999 John switched careers and began working in Harare as a data analyst on HIV/AIDS research and intervention projects for the London School of Hygiene and Tropical Medicine and for Johns Hopkins University. In January 2006 he moved to Stellenbosch to take up the position as inaugural Director of SACEMA, the DST/NRF Centre of Excellence in Epidemiological Modelling and Analysis.

John and his wife Beverley have two children, Daniel and Rebecca.

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Migration, Mines and Mores: The HIV Epidemic in Southern Africa

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Prof John W Hargrove
SACEMA, the DST/NRF Centre of Excellence in Epidemiological Modelling and Analysis
Stellenbosch University

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MIGRATION, MINES AND MORES: THE HIV EPIDEMIC IN SOUTHERN AFRICA

INTRODUCTION

When I was a schoolboy in Bulawayo in 1955 we saw the world through pink tinted glasses; almost everywhere we looked we saw the cheerful pink of colonial British Africa (Fig. 1A): The Union of South Africa, Bechuanaland, South West Africa, Southern and Northern Rhodesia, Nyasaland, Basutoland, Swaziland and further north Tanganyika, Kenya and Uganda.

While, fifty years later, Britain has gone and a lot of the names have changed we still see bright pink all around us (Fig. 1B) though now for rather less cheerful reasons. Now we see the map of southern Africa coloured pink because shades of pink are used by the WHO and UNAIDS to denote levels of HIV infection, with the deepest shades reserved for those countries with the highest prevalence, the most severe epidemics. Ex-British colonies in southern and east Africa are still coloured pink (Fig. 1B), because they have the dubious distinction of constituting eleven of the top fifteen countries in the world in terms of the level at which adult HIV prevalence, in urban centres, peaked in their individual epidemics (Fig. 2).

The other four - Mozambique, Rwanda, Burundi and Ethiopia - are not ex-British colonies, but are also all in southern and east Africa. Although the images in Figs. 1 and 2 are very striking – and although ex-British colonies have an average peak HIV prevalence level 11 percentage points higher than countries with a different colonial past – peak prevalence seems to be more strongly related to region. A simple analysis of variance between countries defined as being southern, east, central or west accounts for 66% of the variance in peak HIV prevalence (Table 1). Countries of southern Africa have, on average, a peak prevalence which is nearly 20 percentage points higher than in the countries of east Africa and nearly 25 percentage points higher than in west and central Africa.

In this lecture I attempt to shed some light on why it should be that the HIV pandemic should be so particularly severe in southern Africa and then consider ideas about what we should try to do to rectify this situation – in the short, medium and long term.

Others have carried out ecological analyses of the pan-African distribution of HIV prevalence. It has been

Figure 1A: Map of sub-Saharan Africa by colonial power, 1955.

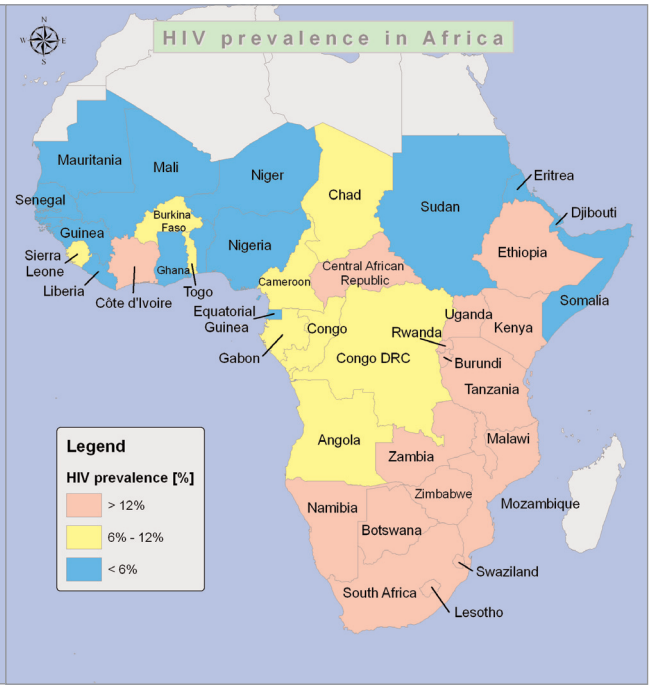

Figure 1B: Map of sub-Saharan Africa by distribution of peak HIV prevalence in urban areas, up to 2007. Data from UNAIDS Fact Sheets.

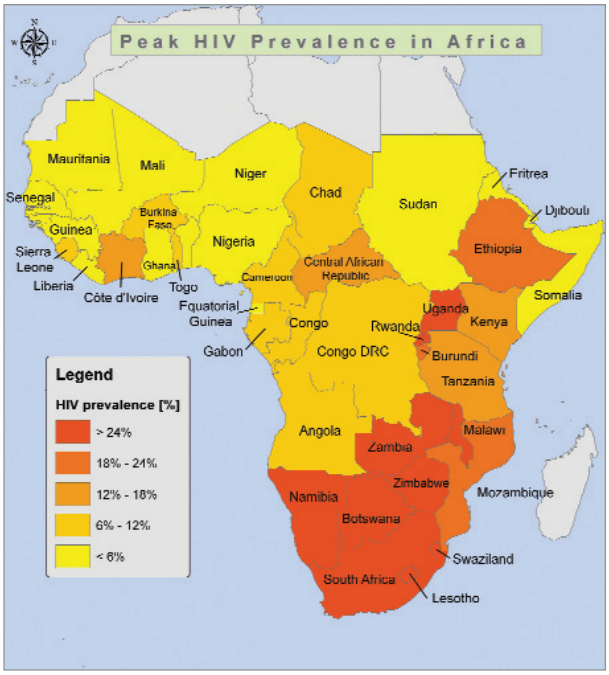

Figure 2: The distribution of peak HIV prevalence levels between countries in sub-Saharan Africa.

shown repeatedly, for instance, that HIV prevalence declines significantly with the proportion of males circumcised in a country (Drain *et al.*, 2004, 2006; Werker *et al.*, 2006). Indeed much of the recent analysis of the distribution of HIV prevalence in Africa has centred on

Table 1: Analysis of variance of peak HIV prevalence by country in four sub-Saharan African regions; $r^2 = 0.66$.

Factor	Coefficient (95% CI; *P*)			
(Constant)	6.4	(2.4,	9.8;	0.002)
Region				
West		[Reference]		
Central	2.6	(-4.1,	9.3;	0.44)
East	8.7	(2.8,	14.7;	0.005)
Southern	26.5	(20.3,	32.7;	<0.001)

adjusting HIV prevalence for various other possible risk factors in order to demonstrate that, having made all of these adjustments, there is still a strong significant protective effect of male circumcision.

By itself, the proportion of males circumcised accounts for about 74% of the variance in peak HIV prevalence as estimated from the UNAIDS 2006 Epidemiology Fact Sheets for urban sites in 42 sub-Saharan African countries (Fig. 3; see also Williams *et al.*, 2006). However, the situation is not nearly as clear when analysis is carried out on countries within the different regions. Univariate analysis within three African regions only produces a significant relationship between HIV prevalence and circumcision rates for east Africa (Table 2). By contrast the proportion of Muslims in a country was a significant factor in each region separately.

We should be clear, however, that the last two

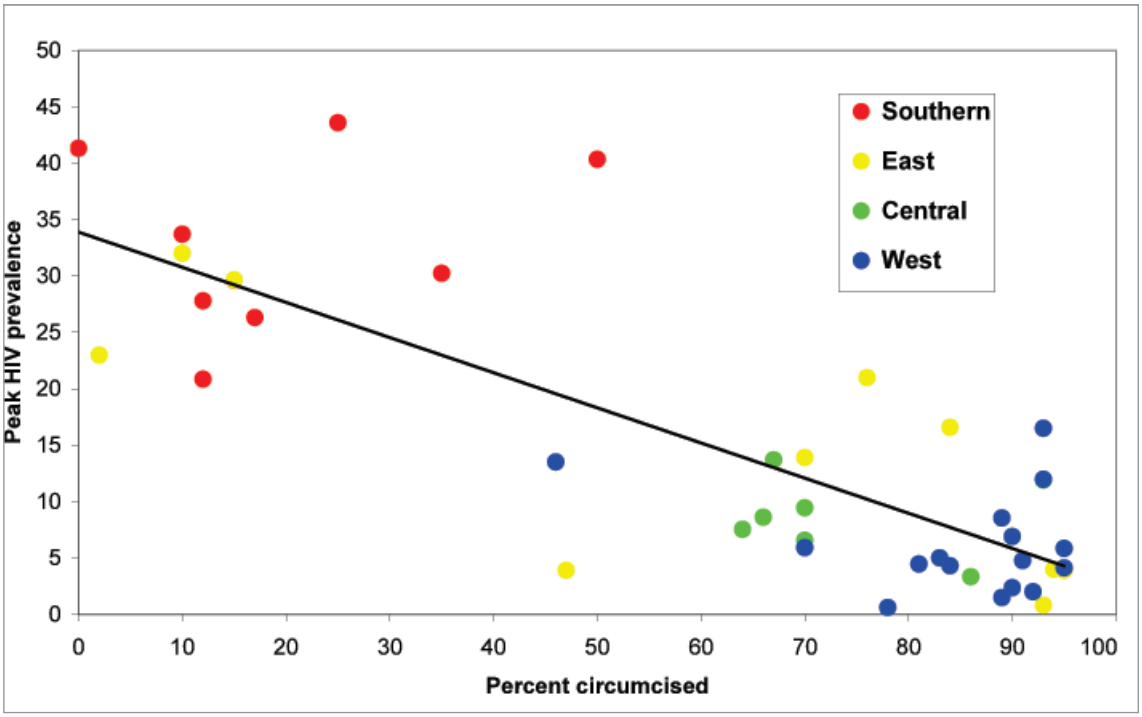

Figure 3: Peak HIV prevalence, as a function of the proportion of men circumcised in the countries of four different regions in sub-Saharan Africa.

Table 2: The relationship between peak HIV prevalence and the fractions of Muslims and of males circumcised by country in various sub-Saharan African regions. With these units, for every 1% increase in the fraction that are Muslim (or males that are circumcised) the prevalence decreases by 1% of the value of the corresponding coefficient. In southern Africa, for example, the decrease would be 0.372% per unit increase in the proportion Muslim.

Region	Fraction Muslim	Fraction Circumcised
	Coefficient (95% CI; r^2; P)	
	Univariate analyses	
Southern	-37.2 (-74.1, - 0.4; 0.37; 0.048)	- 8.6 (-55.5, 38.4; 0.03; 0.68)
East	-31.3 (-46.3, -16.2; 0.71; 0.001)	-29.2 (-42.8, -15.6; 0.72; 0.001)
Central/West	- 7.4 (-12.1, - 2.7; 0.31; 0.003)	-12.8 (-25.8, 0.1; 0.17; 0.052)

years have seen the publication of results from three randomised control trials on the effect of medical male circumcision on the acquisition of HIV infection (Auvert *et al*., 2005; Gray *et al*., 2007; Bailey *et al*., 2007). All agreed in showing a significant protective effect for men; medical male circumcision in each case resulted in at least a halving of the annual rate of new HIV infections. Thus, while ecological studies of the distribution of HIV prevalence in Africa may be open to criticism, the incidence studies provide much more compelling and unequivocal evidence.

The protective effect of male circumcision against the transmission of HIV infection from females to males is thus a less contentious issue than it has been; and the results of the ecological studies referred to above are thus of less interest in this regard. Indeed, given the results in Tables 1 and 2, there is a case for standing the argument on its head. Instead of making adjustments in efforts to demonstrate the protective effects of male circumcision, we could rather adjust for male circumcision and look at the residual variance due to other factors. As we will see, what emerges from this analysis are strong residual regional and religious effects, which suggest what may be important underlying determinants of the HIV epidemic.

COMPARING HIV PREVALENCE LEVELS BETWEEN COUNTRIES

In analysing the distribution of HIV prevalence between countries, it has been the practice to compare prevalences between countries at a single point in time. This has been justified on the grounds that standards of HIV testing have changed, and improved, over the years. It is thus difficult to know how to compare over time prevalence estimates from the same country. Regardless of the problems associated with past estimates of HIV prevalence, however, it is not valid to compare HIV prevalence between countries which are at different stages of the epidemic. A single example should suffice to make this point. In the year 2000 HIV prevalence in urban Uganda was about 8%; in Swaziland it was nearly five times this level at 37%. But this huge difference is entirely due to the timing of the analysis. If the comparison had been done in 1992, for instance, the Swazi HIV prevalence would have been only about 5% and the Uganda prevalence six times as high at nearly 30%.

Given the above, it is clear that analysis of HIV prevalence data, and identification of risk factors using multi-country data, should only be carried out using data from a similar stage of the epidemic in each country. In particular it makes sense to compare the peak levels of HIV. We obtained from the UNAIDS Epidemiology Fact Sheets all available antenatal clinic data on HIV prevalence in urban settings from 42 sub-Saharan countries and fitted the time series of data using a double logistic function. We attempted to ameliorate the variability of these estimates over time, and to reduce the effect of serious outliers in the data, by taking as the peak value the smaller of the observed and predicted peak values of prevalence.

ESTIMATING THE EFFECTS OF MALE CIRCUMCISION AND RELIGIOUS CUSTOMS IN THE SAME MODEL

In an analysis of HIV prevalence in 122 developing countries Drain *et al.* (2004) analysed the effects of male circumcision and religion separately on the grounds that the percent of males circumcised was collinearly correlated with the proportion of Muslim populations. They were thus unable to disentangle the proportion of the protective effect accruing to male circumcision and that accruing to other cultural norms particular to the Muslim faith. In a later paper Drain *et al.* (2006) did try to separate the effects of religion and male circumcision by looking at HIV prevalence in countries stratified on the

basis of the proportion of Muslims (or Christians) in the country. They did not, however, provide a quantitative measure of the protective effect of Muslim behavioural norms other than male circumcision.

In another study a similar analysis noted that the impact of circumcision on the AIDS rate was larger than the impact of the Muslim variable, which included circumcision as well as behavioural norms (Werker *et al*., 2006), apparently implying that no added protection accrues from Muslim behavioural norms. The following development shows that this is not the case.

We define:

γ^m = fraction of Muslim males circumcised = 1

γ^n = fraction of non-Muslim males circumcised

$\gamma^{m,n}$ = overall fraction of males circumcised

μ = proportion of Muslims in the population

We initially set up the model for HIV prevalence (π) as the sum of the effects of the proportion Muslim, the proportion of males circumcised and the region:

$$\pi = a_0 + a_1 \mu + a_2 \gamma^{m,n} + \alpha_3 (R) \quad (1)$$

where a_0 is the intercept in the regression model; a_1 and a_2 are the coefficients giving the decrease in HIV prevalence per unit increase in the percent Muslim and percent males circumcised in the population, respectively; a_3 gives the increase in prevalence in a given region (*R*), relative to the region with the lowest prevalence.

Notice that for an entirely non-Muslim country (*i*. e. when $\mu = 0$):

$$\pi(0) = a_0 + a_2 \gamma^n + a_3(R) \quad (2)$$

from which it is clear that a_2 is the coefficient for the protective effect of being circumcised. Notice that we are implicitly assuming that the protective effect of circumcision is the same for a Muslim as for a non-Muslim man.

In a country which is entirely Muslim (*i*. e. $\mu = 1$ and $\gamma = 1$):

$$\pi(1) = a_0 + a_1 + a_2 + a_3(R) \quad (3)$$

so that the difference in predicted peak prevalence between two countries, one entirely Muslim, and one entirely non-Muslim but where all males are circumcised, (*i*. e. where $\gamma^n = 1$) is given by $\pi(1)$-$\pi(0)$=a_1. Thus the total protective effect of being Muslim (as a result of being circumcised and of other cultural factors) is given by $a_1 + a_2$.

Ideally, since the model in Equation (1) refers specifically to HIV prevalence among the male population, we should be fitting the model to observed levels of HIV prevalence among males. But reliable data on HIV prevalence among males are simply not available at levels sufficient to support a precise analysis. It is reasonable to suppose, however, that the peak HIV prevalence among men in various countries will be highly correlated with the peak prevalence among women in general, and among pregnant women in particular. Accordingly, we apply the above linear model to all available antenatal clinic HIV data from 42 sub-Saharan African countries. Availability of reliable data also suggested the use of data only from urban settings in each country.

RESULTS AND INTERPRETATION OF THE MULTIPLE REGRESSION ANALYSIS

All of the factors offered had highly significant effects on peak HIV prevalence (Table 3) and the inclusion of just three factors accounted for 85% of the variance in the data – despite the inherent variability in, and uncertainty surrounding, the HIV prevalence estimates and the very simple model used to fit the time series for each country. Applying Equation (1) to the results from Table 3, the results are rather straightforward to interpret.

Table 3: Factors associated with peak HIV prevalence in various sub-Saharan African countries. Multiple regression using Equation (1).

		Univariate	Multivariate
	Factor	**Coefficient (95% CI; *P*)**	**Coefficient (95% CI; *P*)**
a_0	Constant		24.2 (17.0, 31.4; <0.001)
a_1	Fraction Muslim	-23.9 (-33.6, -14.2; 0.006)	-9.3 (-15.7, -2.9; 0.006)
a_2	Fraction Circumcised	-35.4 (-42.1, -28.7; 0.001)	-16.0 (-25.5, -6.6; 0.001)
	Region		
a_3	West / Central	[Reference]	[Reference]
	East	7.9 (2.4, -13.5; 0.006)	5.3 (0.9, 9.7; 0.020)
	Southern	25.7 (19.9, -31.5; <0.001)	13.8 (7.5, 20.0; <0.001)

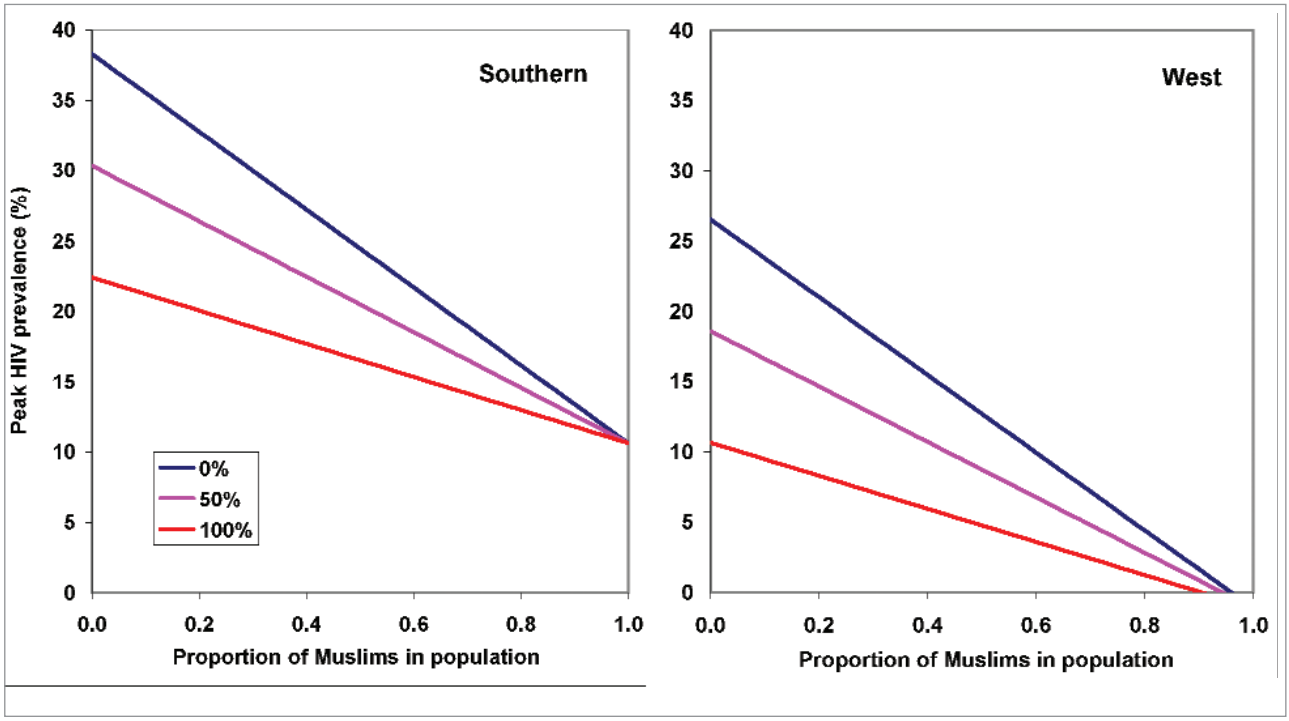

Figure 4: Peak prevalence, as a function of the proportion of Muslims in a country, predicted for various levels of circumcision of non-Muslim males in two regions of sub-Saharan Africa. Predicted values are approximations only: thus, predicted levels of zero (and negative) prevalence for proportions of Muslims close to unity simply reflect the joint effects of data variability and violations of the assumptions inherent in the linear model.

The protective effect of being Muslim can be viewed, crudely speaking, as the sum of protection as a result of male circumcision (a_2 = 16.0), which we assume applies equally to males of all religious persuasion, and protection as a result of other effects (a_1 = 9.3) associated particularly with being Muslim. We should thus predict that an entirely non-Muslim country, and one where no male is circumcised, would have a peak HIV prevalence 16.0 + 9.3 = 25.3 percentage points higher than a Muslim country where all males are, by assumption, circumcised. Notice that, as in an earlier study (Werker *et al.*, 2006), we also see in the univariate analysis (Table 3) that the coefficient for the fraction of male population circumcised is larger than that for the fraction of the population Muslim. But, as we saw above from the multivariate analysis, this does not mean that there is no added protective effect as a result of being Muslim.

These effects are illustrated graphically in Fig. 4, which also illustrates the substantial regional differences in HIV prevalence, when due allowance is made for the proportion of Muslims in the population and of the proportion of men who are circumcised. For the nine countries in the southern region, HIV peaked at 13.8 percentage points higher than in west and central Africa and at 8.5 points higher than in east Africa.

To recap: ecological studies in the past have tended to concentrate on the importance of male circumcision in reducing the risk of HIV infection. There has been a tendency to try to explain regional differences in HIV prevalence rates in terms of male circumcision rates – making the point that countries in southern Africa, which have lower rates of male circumcision than in west Africa, also have much higher HIV prevalence.

The lesson to be learned from Table 3 is rather different. What we see from this analysis is that, even when we adjust for male circumcision rates and indeed for the proportion of Muslims in various countries, we still find that HIV prevalence in southern Africa is very much higher than in the rest, particularly the west, of Africa. What the analysis also says is that even after adjustment for male circumcision rates there is a still a strong protective effect as a result of being Muslim, nearly 60% of the protective effect of male circumcision and, statistically, not differing from it significantly.

And these two results must surely raise in one's mind the obvious question: "Is there some common factor that we can see, which might simultaneously explain why the risk of HIV infection is so much lower in Muslim communities and so much higher among all countries in southern and, to a lesser extent, east Africa?"

In the ecological studies of Drain *et al.* (2004, 2006) many factors are considered as possible risk factors for HIV infection and, at least in univariate analyses, many statistically significant effects were found: population density, female literacy, poverty, skewed wealth distribution, the proportion of young people in a country, human development index, sexual behaviour patterns such as divorce, polygamy and fertility rates and age at first intercourse, co-infection with other sexually transmitted diseases and tuberculosis, and a large number of variables related to health and health services immunisation rates, the numbers of doctors in a country, and various measures of sexual behaviour.

But, in multivariate modelling, the only factors among those listed above which had statistically significant effects were: i) the proportion of young people in the population, which was positively correlated with HIV prevalence; ii) immunisation rates, female literacy levels, and numbers of doctors per head of population - which were all negatively correlated with prevalence. None of these factors seems to fit the requirement of being simultaneously responsible for particularly raised HIV prevalence in southern Africa and the reverse in predominantly Muslim countries. Other factors of potential importance have, however, been ignored in the analyses cited. Thus, in a little-quoted paper dating from 1991, my fellow Zimbabwean, David Sanders and Abdulrahman Sambo argued that "the migrant system of labour in southern and east Africa contributes to family separation and the spread of disease (including AIDS), from urban to rural areas as well as in the opposite direction" (Sanders & Sambo, 1991; *p* 158).

In the ecological studies mentioned above there is no consideration of such effects.

On the one hand this is not entirely surprising since data on relative levels of family coherence, and of urban/rural movements are difficult to quantify and to compare between African countries. On the other hand, family coherence seems a feature that is very strong in Muslim culture and one that has also been particularly severely compromised in southern Africa. Bearing in mind the results encapsulated in Table 3, therefore, family structure, and factors which impact on that structure, may provide important keys to an understanding of the distribution of HIV infection in Africa. It is therefore worth considering some details of the historical development of southern African society, the consequent impact on family structure and how this may be related to the HIV pandemic.

RHODES NOT ROADS

When considering family separation and migration in southern Africa the word "Apartheid" perhaps jumps into your mind – Apartheid is a favourite whipping boy in discussions of the roots of all evil in southern Africa in general and for the HIV epidemic in particular (Lurie, 2000). There can be no doubt that Apartheid contributed greatly to the breakdown and fragmentation of social and family life in South Africa, but I think the problems have much older and rather different origins as I shall explain shortly.

Similarly, when one thinks of the role that the movement of people has played in the spread of HIV there was in the past (Carswell *et al.*, 1989), and sometimes still is, a tendency to demonise truck drivers. Parallels were drawn between good road systems and the rapid spread of the virus via commercial sex workers at truck stops. Roads and road transport undoubtedly played a role, but the analysis above suggests a quite different villain; it's not *roads* we should be thinking of, rather we should be thinking of *Rhodes*. Cecil John Rhodes. Because it was Rhodes, Alfred Beit and their mining associates, aided and abetted by Lord Alfred Milner, who sowed the seeds of the southern African HIV epidemic – and many other problems that are essentially sociological in nature. Let me explain.

In 1884, following the defeat of British forces at Majuba, Paul Kruger signed, under duress, the Convention of London which gave the Transvaal independence in all matters except control over its foreign affairs. What neither side was to know was that gold would be discovered in the heart of the quasi-independent territory just two years later. Gold in unprecedented quantities; and gold which Kruger's volk were not then in a position to mine and exploit fully for themselves. Most people here will know better than I what then developed. I note only that, according to one analysis, it was essentially Milner's efforts, helped particularly with funding from Beit, that heaped unbearable diplomatic, and then military, pressure on Kruger – making demands which Milner prayed Kruger would reject (Pakenham, 1979). Ultimately the pressure told on Kruger, who seems to have been persuaded by Smuts that, if it had to be war, then the Transvaal should strike first. The Transvaal sent the British an ultimatum and, when it expired, invaded Natal. Milner's prayers had been answered – though the less than edifying period in British colonial history which followed was perhaps not quite what Milner had in mind.

For Milner, and Rhodes, the battle had always been about "Empire"; but the real impetus behind the battle

in South Africa was the gold. And, putting aside the rights and wrongs of the Anglo-Boer war, the subsequent explosive expansion of the goldfields led to massive development in South Africa and further finance for commercial expansion into the neighbouring territories funded in large part by people like Rhodes and Beit.

And it wasn't just the material wealth that Rhodes and company needed from the neighbouring countries. Because there was a major problem with the gold on the rand. The geologists quickly found that most of the gold was deep underground – and the deeper the gold the more expensive it was to mine. All costs had to be kept to a minimum; and labour costs, in particular, had to be cut to the bone, especially because the demand for labour was huge. As a consequence the South African mines needed manpower from neighbouring countries. And I do mean "man" – not the more politically correct "person"; women were almost entirely excluded from the equation. There could be no question of having black *families* living on the rand; only the males could do the heavy work underground, so only males would be housed.

And housed they were; hundreds of thousands of men at any one time all over the Transvaal and then the Orange Free State. Not just from South Africa, but from Southern Rhodesia, Northern Rhodesia, Nyasaland, Mozambique, South West Africa, Swaziland and Basutoland. Over the years companies such as "Wenela" brought millions of healthy, strong and virile young men for a stint on the mines. Their wives and womenfolk were at home all over southern Africa; they saw each other perhaps only once a year. In between times … well, I don't have to tell you what strong, virile young men are wont to do – particularly when they have rather more money than their peers in general and young ladies in particular. And what of their wives and girlfriends left at home for months at a time? It was a catastrophe waiting for something like an HIV virus to come along.

We should not single out only the mines, and certainly not just the South African mines, as the sole villain of the piece. As Sanders and Sambo (1991) point out, the British tried to use forced labour in Uganda, and later recruited Rwandans and Malawians to work there on the coffee and tea estates. And the principle of having males only living and working on mines, as well as on farms and plantations – and even as domestic workers in big cities – became the norm all over British southern, and to an extent, eastern Africa. The pattern was more or less similar everywhere from the Cape through the Rhodesias, Tanganyika and to the "White Highlands" of Kenya. In cities in Southern Rhodesia, until well into the 1960s, it was illegal for a (white) employer to allow his (black) manservant to have his wife living on the premises with him.

THE EPIDEMIOLOGICAL CONSEQUENCES OF OSCILLATORY MIGRATION PATTERNS

What became entrenched was a system where, typically, men lived and worked in cities or on large estates; they returned, perhaps only once or twice a year, to their wives and families, who typically had to maintain a foothold in the countryside, farming a small piece of land, with little support.

While there is little, if any, direct evidence to link this system of oscillating migration and the resulting damage to family structure to its epidemiological consequences, we can offer some indirect evidence. Using a diffusion model for the spread of an infection like HIV it is easy to demonstrate the intuitively obvious fact that even high levels of sexual activity, and partner change, leads to surprisingly low rates of epidemic expansion – as long as all of this sexual activity is also strictly localised. An African version of *Peyton Place*, or *Desperate Housewives*, if you prefer. Thus, while concurrent relationships (Epstein, 2007) may well be important necessary conditions for building an epidemic they are not sufficient. What we also need is that the partners, concurrent or not, are geographically separated.

The modelling shows that if even 10% of a person's sexual activity is directed in a geographically distant location the spread of the epidemic is spectacularly different (see graphic in Supplementary Methods for this lecture on www.sacema.ac.za). This model, which mimics the essential features of oscillating migration, also suggests why such migration is an essential component for an epidemic to be as severe as the one we are witnessing in southern Africa.

Even within the southern African HIV epidemiological epicentre there are indications that those people who have the strongest family structures and psychosocial support systems are also least likely to acquire HIV infection.

Multivariate analysis of HIV prevalence data from Harare, Zimbabwe (Table 4) shows that women who are HIV-infected are more likely than HIV-negative women to be unmarried, have not completed secondary school education, rent or live with extended family rather than own their home, be unemployed, have a husband with fewer years of schooling and a

Table 4: Regression analyses of risk factors for prevalent HIV infection among postpartum women enrolled in ZVITAMBO trial. Also adjusted for date of recruitment, age and parity

Variable		*n*	Odds ratio (95% confidence interval)
Marital status	Married	13 198	1
	Single	638	1.36 (1.13, 1.63)
	Divorced	174	1.54 (1.13, 2.11)
	Widowed	100	3.97 (2.53, 6.23)
Mother's religion	Non Catholic	10 643	1
	Catholic	2709	1.19 (1.09. 1.31)
	None	705	1.31 (1.11, 1.55)
Mother's education	Secondary	11 515	1
	<Secondary	2542	1.58 (0.99, 2.53)
Father's education	Secondary	12 701	1
	<Secondary	1356	2.27 (1.25 - 4.13)
Father's occupation	Profession	2306	1
	Other	11 751	1.22 (1.10, 1.35)
Mother's housing	Own	1464	1
	Other	12 593	0.43 (0.24, 0.77)
Family income (US$/mo)	≥18	10 332	1
	< 18	357	1.45 (1.16, 1.82)
	Missing	3378	1.18 (1.08, 1.29)

non-professional occupation, and have an extremely low family income and no religious affiliation (Humphrey *et al*., 2007).

Low income of itself was less important than other factors, being only associated with increased HIV-1 prevalence among women with the lowest 3% of incomes. In short, what seemed to be important was the strong "psychosocial support" typical of a settled family lifestyle.

THE LONG-TERM SOLUTION

Regardless of anything else I say below, the preceding analysis supports very strongly the ideas advanced by Sanders and Sambo (1991) that the HIV pandemic in this part of the world has its roots in structural deficiencies – and not in the inherently aberrant sexual behaviour wrongly attributed to African populations. That paper, published in 1991, was remarkable in that the HIV prevalences rates at that time in the urban areas of Botswana, Lesotho, Swaziland and South Africa were "only" 8%, 5%, 2% and 4%, respectively. How much more powerfully can the point be made today when the prevalence levels are 6 to 15 times higher in these southern African countries (UNAIDS Epidemiology Fact Sheets, 2006). Sanders and Sambo did not explicitly predict the tsunami of HIV that was about to overwhelm South Africa and its immediate neighbours south of the Limpopo but, given that they identified so accurately the structural deficiencies that seem so self-evidently important in the development of the epidemic, the prediction was almost inescapable for those countries that have been the most severely affected by the oscillating migration associated with the mines, farms and cities of southern Africa.

The inescapable conclusion must be we need to address urgently the issue of how we can rebuild family structures in southern and eastern Africa. Without that change we may confidently predict extreme difficulty in dealing effectively not only with the HIV epidemic, but also with many other problems having similar sociological determinants.

CHANGING HIV PREVALENCE AND INCIDENCE IN ZIMBABWE

Given the extreme difficulty involved in changing sociological patterns, particularly employment practices that have been entrenched for more than 100 years – and practices that are implicitly so beneficial for big business (regardless of the language spoken by the bosses or the colour of their skins) – one must conclude that sociological improvement will be slow in coming.

The essential structural elements that predispose southern Africa to disastrous levels of HIV infection and other social ills are therefore likely to remain largely intact for the foreseeable future. Given that reality, can there be any ray of light, any glimmer of hope, in what is now the epicentre of the pandemic? Curiously, I think there is – even within the very heart of darkness. Despite all the economic, social and legal shambles, and the human rights abuses that characterise Robert Mugabe's Zimbabwe (Todd, 2007), we see the curious fact that HIV prevalence among women attending antenatal clinics (ANCs) in Harare has been declining at nearly 10% per annum since about 1998 (Fig. 5) (Mahomva *et al.*, 2006). Moreover, basic epidemiological principles suggest that HIV incidence – *i.e.* the rate of occurrence of new infections – started to decline in 1994. Mathematical modelling (Hallet *et al.*, 2006) suggests that these declines could not be attributed solely to the direct effects of increased deaths among HIV-positive individuals, but were associated with declines in HIV incidence and changes in sexual behaviour.

Hallet *et al.* (2006) fitted the Zimbabwe ANC data for 2000-2004 with a model that sees risky sexual behaviour halving after 2000, though they do not suggest why, or how, such a decline in incidence might have arisen. From more extensive Harare ANC data it appears, however, that HIV prevalence among younger (<24 years old) women has actually been declining since 1994. Since the vast majority of the HIV-positive members of this age group must have been infected relatively recently, this suggests that the decline in incidence, and reduction in risky behaviour, started as early as 1994.

That is not to diminish the importance of death in the changing face of the HIV epidemic. HIV incidence will decline as a natural direct consequence of the early attrition of that class of society exhibiting the riskiest sexual behaviour. If there is no accompanying change in human behaviour, however, the incidence soon levels off and equilibrium is established where the death rate matches the rate of occurrence of new infections and the HIV prevalence is maintained at a high level.

But death can also have an indirect effect on HIV incidence prevalence if human beings react to the manifest effects of the HIV epidemic by changing their behaviour. And the evidence of massively increased death rates in the recent past is all too manifest in Harare. An area of 150 hectares just south of Harare that was bush just ten years ago is now a massive cemetery with tens of thousands of closely packed graves (Supplementary Material).

Mathematical modelling shows that it is possible to produce a good fit to the HIV prevalence in Fig. 5 under the assumption that the rate of occurrence of new infections decreases as the observed death rate increases. The best fit of the model to the HIV incidence and prevalence data suggests, moreover, that the death rate should have peaked in about 2001/2, as indeed appears to be the case from the records of deaths in Harare.

The fit is thus consistent with the not unreasonable contention that people have modified their behaviour according to the death rate at any given time. The particular mathematical assumption that incidence declines exponentially with death rate does, however, come with the consequence that reductions in risky behaviour lead to declines in the death rate – and thus, by our model, subsequent increases in risky behaviour. The predicted incidence, prevalence and death rates thus level off instead of continuing to decline steadily (Fig. 5). The model does not, in other words, attribute any "memory" or "learning behaviour" to the individuals modelled. Levels of risky behaviour simply increase or decrease mechanically as a simple inverse function of the death rate.

On the one hand it is to be hoped – and this is my expectation – that this is an unduly misanthropic view of humankind, and that people will actually be (even) more thoughtful in their response to the observed effects of HIV than suggested by our model. Conversely, many would view mine as an unrealistically optimistic view of the world. Indeed the suggestion that HIV incidence has indeed been declining in Harare, and that this must be due to changes in behaviour, has met with great scepticism from some scientists. One is left with the feeling that they find it hard to believe that people are capable of altering their sexual behaviour – except perhaps

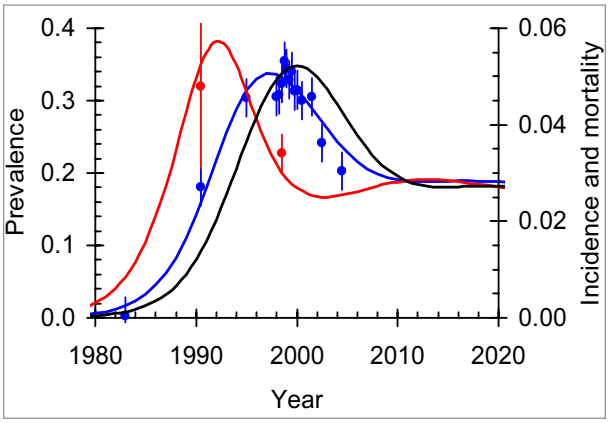

Figure 5: Estimated (dots) and fitted (curves) HIV incidence (red) and prevalence (blue) and deaths (black) among women attending antenatal and maternity clinics in Harare, Zimbabwe (Data from Mahomva *et al.*, 2006).

through enlightened government policy, or via the insightful intervention by a generously funded international organisation.

Judith Todd takes a more optimistic view of human behaviour (Todd, 2007). She notes that Zimbabweans overwhelmingly rejected Ian Smith's offer of a political settlement in 1972, brokered by the British government via the Pearce Commission. In 2000 they, similarly, overwhelmingly rejected Robert Mugabe's offer of a new constitution which brought promise of free farm land. The leadership in both cases drew the conclusion that the electorate was politically naïve and easily led astray by the unscrupulous; black nationalists in the first instance – white farmers in the second. Todd, who has been cruelly persecuted under both governments, drew a quite different conclusion; she argues that, in both cases, the people very accurately detected evil intent and rejected it.

Perhaps that same simple human intelligence, rather than the efforts of governments and aid agencies, is the most important factor underlying the decline in HIV prevalence seen not only in Harare, but also in Uganda and increasingly in other countries in the region (Hallet *et al*., 2006). And perhaps governments and aid agencies find this pill so hard to swallow because it so diminishes our efforts. Nonetheless, if true, what the message implies is that the most important role of the scientist remains exactly as it has been for millennia – the objective and accurate dissemination of information.

THE DEVELOPING HIV EPIDEMIC IN SOUTH AFRICA

This more optimistic view might appear at first sight to find little support from the observed development of the HIV epidemic in South Africa - where by 2006 there is still no evidence of the beginnings of the rapid decline in HIV prevalence observed in Harare (Fig. 6) - despite the abundant and direct evidence everywhere in South Africa of the effects of HIV infection. It is true that HIV prevalence for 2006 was marginally (though not significantly) lower than for 2005 (Fig. 6) and estimates from the ASSA model (Dorrington et al., 2006) suggest that HIV incidence has started to decline. It is also true (Fig. 6) that the epidemic in South Africa lags the Zimbabwean epidemic by about eight years, so that it is possible (though not in the least guaranteed) that we might be about to witness a similarly sharp decline in HIV prevalence in South Africa.

Nonetheless the present levels of HIV infection are entirely unacceptable. Even in Zimbabwe, where HIV prevalence appears to have been declining rapidly for at least six years, the last published estimates of HIV prevalence in Harare ANCs was still about 20% (Fig. 5) – hardly a healthy situation. Much the same can be said of other southern African countries and so we need to ask what, if anything, we can do to influence this situation in a positive manner.

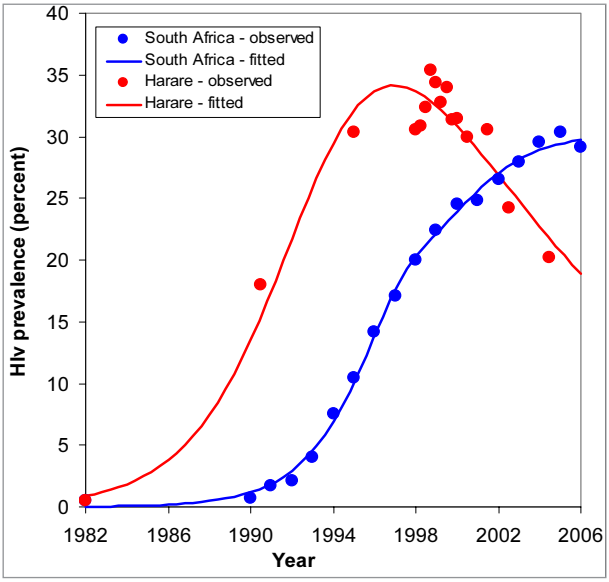

Figure 6: HIV prevalence among women attending antenatal and maternity clinic in Harare, Zimbabwe (Mahomva *et al*., 2006) and South Africa (UNAIDS Epidemiology Fact Sheets, 2006).

ONE SMALL SNIP FOR MAN …

There is evidence in some instances of HIV prevalence and incidence declining as a consequence of behavioural change. This has sometimes been attributed to direct governmental action – as was argued when the Thai government pressured female sex workers to use condoms with their clients (Nelson *et al*., 1996). Similarly Stoneburner and Low-Beer (2004) attribute declining HIV prevalence in Uganda during the 1990s to "population mobilization", which involved the efforts of central government and civil society. The importance of external intervention, other than education regarding the nature and dangers of HIV, is unclear. The declines in HIV incidence and prevalence in Zimbabwe, for instance (Fig. 5), have been of a similar order to those observed in Uganda – but have not been linked to intervention on the scale attributed to the governments of Uganda or Thailand. This area continues to be a matter of debate.

What is not a matter of debate is that there is currently very little by way of alternative options in the drive to reduce HIV incidence. Whereas very large

sums of money continue to be invested in the development of HIV vaccines, and of microbicides that could be used to block infection chemically, the sad truth is that there is no chemical product of any kind that is currently useable to reduce HIV incidence. Indeed organisations centrally involved in the production of such chemicals are of the opinion that we are years away from delivering even a partially effective vaccine or microbicide (AVAC, 2007).

In the light of the absence of viable chemical protection, the recent publication of the results of three randomised control trials demonstrating a more than 50% protective effect of male circumcision on female-to-male transmission of HIV (see references above) is a matter of importance. Mathematical modelling suggests that a full-scale roll-out of male circumcision in sub-Saharan Africa could avert 2.0 (95% ci 1-3.8) million new HIV infections and 0.3 (95% ci 0.2-0.5) million deaths over the next ten years. Over the ten years thereafter a further 3.7 (95% ci 1.9-7.5) million new HIV infections and 2.7 (95% ci 1.5-5.3) million deaths could similarly be averted.

The above modelling involved contributions from several SACEMA associates, and SACEMA has from its inception taken an active interest in the development of male circumcision as an intervention and continues to support Prof Bertran Auvert in his development of both the theoretical and practical aspects of the work.

The success of the intervention as modelled above depends, of course, on the assumption that the natural reduction in the probability of female-to-male transmission of the HIV virus in circumcised men is not offset by increases in risky behaviour tending to reduce, nullify or even over-compensate for the protective effect. The only way to find out is to move towards a more general roll-out of male circumcision as an intervention method and, crucially, to follow the circumcised men to compare their HIV incidence relative to men in the general population.

SACEMA fully supports the idea of expanding the application of medical male circumcision in South Africa: as a natural follow-up to randomised control trials, such operational research will allow the further assessment of the challenges associated with applying the procedure on larger scales, whilst providing the necessary time to assess the longer-term protective effects.

Further indications of the protective effects of medical male circumcision would inevitably influence cultural leaders of non-circumcising ethnic groups to reassess their attitudes to the practice. Moreover, even among groups who do habitually circumcise their males it may lead to a re-assessment of the timing and means of male circumcision. It has been noted that the absence of clear differences in HIV prevalence rates between South African ethnic groups who do, and do not, circumcise their males may be related to the manner in which the circumcision is carried out. Medical observers note that traditional male circumcision can remove variable amounts of the foreskin and that, therefore, the protective effect of traditional male circumcision against HIV infection may be less than optimal.

If the observed ongoing results of increased frequency of medical male circumcision are sufficiently positive, the medical fraternity may need to start asking questions about whether they should be advising parents of all ethnic groups to have their sons medically circumcised at birth as a matter of course. To the objection that this flies in the face of long-standing cultural values, one may counter quite simply that cultures do, and should, change: and there is no better reason to change than in the interests of survival. Regardless of the changes which do, or do not, occur with regard to future male circumcision practices, what is of paramount importance is that all male circumcisions should be carried out with the utmost regard to safety for the patient.

ANTIRETROVIRAL THERAPY AS AN OFFENSIVE WEAPON

The above discussion of methods available for reducing HIV incidence and prevalence has centred on prevention of infection. With double-digit HIV prevalence levels throughout southern Africa, however, we have massive numbers of people who are already infected with HIV. There has, quite rightly, been increasing pressure over the years to improve access to antiretroviral therapy – with the major emphasis on the improved survival and quality of life of the patient, consistent with considerations of delaying treatment so as to lessen the time spent on drugs which can have unpleasant side-effects and simultaneously reducing costs and the chances of developing resistance. These arguments are used to justify the standard practice in Africa of starting ART only when the CD4 count drops to 200, or when an HIV positive patient presents with symptoms typical of a WHO stage 3 or 4 infection.

There are several problems with this approach:

i) As a patient's CD4 count declines the probability of acquiring opportunistic infections increases. In particular, by the time the count approaches 200 many will already have TB – which has to be treated before ART can commence:

ii) Even if the patient has not acquired TB, if the CD4 count is below 200 at the onset of ART this count does not fully recover in some patients. While the *mean* CD4 count increases, the increase in the *mode* is less impressive, and there is a proportion of patients whose CD4 count remains below 200:

iii) Even after three years on ART the probability of infection with TB is several times higher than in HIV negative people:

iv) These results are consistent with suggestions that prolonged infection with HIV leads to accelerated senescence of the immune system (Appay *et al.*, 2007).

While none of these lines of evidence may be compelling by itself, together they do constitute an argument in favour of a markedly earlier onset of antiretroviral therapy – in the interests of the individual HIV positive patient. And there is a further important epidemiological reason for wanting to start therapy earlier. Analysis of data from one study in the Cape showed that, whereas the roll-out was reaching seven times the national average in terms of the proportion of patients on ART among those who qualify, the HIV positive patients who were not enrolled into ART therapy were predominantly people under 30 years of age. On the one hand, this is entirely natural since the youngest people tend, by definition, to have been HIV positive for the shortest time. Thus the proportion with a CD4 count less than 200 is smaller than in older age groups. On the other hand, the young are the most sexually active age group and thus the most important target for any programme that aims to reduce transmission rates. Earlier onset of ART would have the important and natural epidemiological effect of reducing the viral load in larger numbers of sexually active patients and would thereby automatically reduce the probability of this group infecting their sexual partners. It seems, therefore, that there is a convergence of the individual and population interests in the early recruitment of HIV-positive patients into ART programmes.

If modelling indicates that the aggressive use of ART in this way could be of service in reducing HIV incidence, there may be a further argument for a more active approach towards the identification of HIV-positive cases such that major reductions in viral load can be effected in the greatest proportion of HIV-positive people. While political considerations currently prevent general compulsory HIV testing, it is interesting to note that Botswana has already moved to an "opt out" approach to HIV testing. That is to say that anybody visiting a clinic can automatically be given an HIV test – unless they specifically ask not to be tested.

CONCLUSION

I have mentioned above various possible measures aimed at addressing the immediate problem of reducing HIV incidence in South Africa: earlier roll-out of antiretroviral therapy, coupled with a more aggressive approach to case detection and promotion, and proactive promotion of male circumcision. Any such intervention will have to be combined with education programmes concerning the reasons for male circumcision and especially the fact that it gives partial but not complete protection so that the use of condoms must still be strongly promoted. The roll-out of ART will have to be combined with education and counselling especially in regard to protecting one's partner and future children but may also serve as a way of encouraging people to come forward for testing. These interventions will need very substantial commitment and financial resources and much of the responsibility for this will fall on the shoulders of government. There will undoubtedly be debate about the wisdom of these approaches but, even if they are as successful as we hope they will be, one needs to be mindful of the fact that they essentially amount to the management of an immediate crisis.

None of these interventions – nor previous efforts to encourage abstinence, fidelity or condom use – address the fundamental social problems which have ensured that the HIV epidemic would be so severe in the southern African region. Indeed AIDS in southern Africa should be seen not only as a disease but also as a symptom of social ills in general, and of the fragmentation and breakdown of family life in particular. If the analysis presented here has any validity at all, what it implies is that until we manage to address the underlying problem of the breakdown of family structure in the region – and in South Africa in particular – we must expect that our populations will continue to be prey to HIV and to any new sexually transmitted infection which arises.

Nor is the problem restricted simply to sexually transmitted infections. South Africa currently has one of the highest rates of violent crime in the world. There are twice as many murders in a year in Cape Town as there are in the whole of England and Wales. One can point a finger at inadequate policing, corruption and a general lack of political will in combating crime. But it is tempting to suggest that high crime levels and the high incidence of HIV infection have the same underlying structural source – the breakdown of family structure associated with oscillating migration.

In combating HIV-AIDS there is, of course, a continuing imperative for scientific innovation, for education

and mobilisation involving religious, community and political leadership, and for increased efforts in providing effective treatment for those already infected. But, the underlying cause of the HIV epidemic, and of many of our social ills, has its roots in policies set in motion more than a century ago. The present government is not responsible for those policies. They are, however, in the unenviable position of having inherited the responsibility for the consequences – and therefore need to mobilise all appropriate help in addressing the underlying cause of the HIV epidemic in South Africa.

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